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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,995	07/09/2001	Didier Branellec	ST98032	1245

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,995	BRANELLEC ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *plasmid map pASN286-56.*

DETAILED ACTION

This office action is in response to an amendment filed 11/24/03. Claims 21-23 have been added. Claims 1-16 and 19-23 are pending.

Priority

The instant application appears to claim benefit of an International application PCT/FR99/02265. However, the filing date of this application is listed as 9/25/99 in the oath, which contradicts the filing date listed on the application data sheet (ADS), which lists 9/23/99. The ADS will govern when inconsistent data is supplied (see MPEP 601.05).

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 7-16 and 19-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Antelman et al. US 6,074,850 (Jun. 13, 2000 filed Feb 14, 1997). **This rejection is maintained for reasons of record in the office action filed 7/29/03 and maintained below. This rejection is extended to newly added claims 21-23.**

Antelman et al. teach a viral vector or plasmid for tissue specific expression of an E2F-Rb fusion construct (column 15, line 5-9). This fusion contains genes able to induce apoptosis, modify proliferation and that function as transcription factors. This plasmid, pASN286-56, contains the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and an E1A

enhancer followed by the human smooth muscle α-actin promoter and a 286-56 cassette (containing the fusion of E2f and Rb) followed by the E1b/proteinIX poly A signal (column 15, line 26-31). Antleman et al. teach pharmaceutical formulations for the administration of the adenovirus by formulation of liposome suspensions acceptable for intravenous or local or topical administration (column 10, line 35-64).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antelman et al. US 6,074,850 (Jun 13, 2000) in view of Boshart et al. Cell (1985) 41:521-530. **This rejection is maintained for reasons of record in the office action filed 7/29/03 and maintained below. This rejection is extended to newly added claims 21-23.**

Applicants claim a hybrid promoter comprising an enhancer region and a promoter region that directs high expression in smooth muscle cells. The enhancer is selected from the group consisting of the CMV enhancer region, the RSV-LTR enhancer region SV40 enhancer region and the EF1α enhancer region.

Antelman et al. teach a viral vector or plasmid for tissue specific expression of an E2F-Rb fusion construct (column 15, line 5-9). This fusion contains genes able to induce apoptosis, modify proliferation and that function as transcription factors. This plasmid, pASN286-56,

contains the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and an E1A enhancer followed by the human smooth muscle α-actin promoter and a 286-56 cassette (containing the fusion of E2f and Rb) followed by the E1b/proteinIX poly A signal (column 15, line 26-31). Antleman et al. teach pharmaceutical formulations for the administration of the adenovirus by formulation of liposome suspensions acceptable for intravenous or local or topical administration (column 10, line 35-64).

The primary reference does not teach use of the CMV enhancer in the smooth muscle cell specific vector, pASN286-56, which utilizes the E1A enhancer.

Boshart et al teach isolation and characterization of the CMV enhancer. The CMV enhancer was found to be the strongest enhancer analyzed (page 42, column 2, first paragraph). Boshart et al. found that the enhancer has little cell-type or species preference for enhancement of expression and is a useful component of eukaryotic expression vectors (abstract). This was shown by enhanced expression of rabbit β-globin using the CMV enhancer. Therefore, the CMV enhancer, similar to the E1A enhancer, enhances expression of heterologous genes in a strong and ubiquitous manner.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the E1A enhancer in the expression vector taught by Antelman et al. with the CMV enhancer taught by Boshart et al. because Antelman et al. teach that it is within the ordinary skill of the art to use a smooth muscle specific vector and because Boshart et al. teach that it is within the ordinary skill of the art to use a CMV enhancer as a heterologous enhancer. One would have been motivated to do so in order to receive the expected benefit of enhanced expression from pASN286-56 by the use of the CMV enhancer in the vector. Based upon the

teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

On page 8-10 of the amendment filed 11/24/03, applicant traverses the rejection of claims 1-16 and 19-20 under 35 U.S.C. 102(e) and 103. Applicants argue that Antelman et al. contain insufficient information on the synthesis of plasmid pASN286-56 to enable one of skill in the art to determine the sequence of the plasmid in general or the sequence or size of the space between the promoter and the enhancer. As Antelman teaches that the promoter follows the enhancer and the spacial relationship between promoters and enhancers can vary widely with enhancers being of greatly varied distances between upstream and downstream promoters one of skill in the art could not conclude from the Antelman disclosure that the enhancer and promoter of pASN286-56 are within 1kb of each other.

Applicant's arguments filed 11/24/03 have been fully considered but they are not persuasive. Antelman et al teach "This plasmid (pASN286-56) consisted of the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and E1a enhancer, followed by the human smooth muscle α-actin promoter an, 286-56 cassette, and then Ad 2 sequence 4021-10462 (which contains the E1b/protein IX poly A signal) in a pBR322 background." (column 15,line 26-31). This hybrid promoter is comprised of an enhancer and a promoter functional in smooth muscle cells with no intervening sequences between the two. Therefore the enhancer and promoter are less than 1 kb apart. This is conveyed in the plasmid map which is attached to this

office action and confirms that the hybrid promoter is as described, with no intervening sequences between the enhancer and promoter. Therefore, the plasmid of Antleman et al. meets the limitations of the instant invention.

Conclusion

No claims allowed.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571) 272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571) 272-0278. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, whose telephone number is (703) 308-0196.

Maria B Marvich, PhD
Examiner
Art Unit 1636

January 29, 2004

GERRY LEFFERS
PRIMARY EXAMINER